

We claim:

1. A method for pre-sensitizing cancer prior to a therapeutic treatment, comprising the step of:  
  
administering a therapeutically active amount of a serum-free and mitogen-free cytokine mixture to cancer.
2. The method of claim 1, wherein said therapeutic treatment is selected from the group consisting of chemotherapy, immuno-therapy and radiation therapy.
3. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 20 IU to 1600 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
4. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 40 IU to 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
5. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period

in a range from about 35 IU to 75 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.

6. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 55 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
7. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 400 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
8. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
9. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered five times a week over a two week period

at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.

10. The method of claim 1, wherein said serum-free and mitogen-free cytokine mixture is comprised of specific ratios of cytokines selected from the group of IL-1 $\beta$ , TNF- $\alpha$ , IFN- $\gamma$  and GM-CSF to Interleukin-2 (IL-2) as follows:
  - IL-1 $\beta$  to IL-2 at a ratio range of 0.4 – 1.5;
  - TNF- $\alpha$  to IL-2 at a ratio range of 3.2 – 10.9;
  - IFN- $\gamma$  to IL-2 at a ratio range of 1.5 – 10.9; and
  - GM-CSF to IL-2 at a ratio range of 2.2 – 4.8.
11. The method of claim 10, wherein said specific ratios of cytokines are as follows:
  - IL-1 $\beta$  to IL-2 at a ratio range of 0.6 to 0.8;
  - TNF- $\alpha$  to IL-2 at a ratio range of 7.7 to 11.3;
  - IFN- $\gamma$  to IL-2 at a ratio range of 4.9 to 7.1; and
  - GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.
12. The method of claim 1 wherein the serum-free and mitogen-free cytokine mixture is Multikine®.
13. A method for inducing tumor cells into a cell cycle selected from the group of G<sub>1</sub>,

S, G<sub>2</sub> and M , comprising the step of:

administering a therapeutically active amount of a serum-free and mitogen-free cytokine mixture to a cancerous cell.

14. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 20 IU to 1600 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
15. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 40 IU to 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
16. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period in a range from about 35 IU to 75 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.

17. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 55 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
18. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 400 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
19. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered three times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
20. The method of claim 13, wherein said serum-free and mitogen-free cytokine mixture is peritumorally administered five times a week over a two week period at 800 IU wherein IU represent International Units for Interleukin-2 given in World Health Organization 1<sup>st</sup> International Standard for Human IL-2, 86/504.
21. The method of claim 13, wherein said serum-free and mitogen-free cytokine

mixture is comprised of specific ratios of cytokines selected from the group of IL-1 $\beta$ , TNF- $\alpha$ , IFN- $\gamma$  and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1 $\beta$  to IL-2 at a ratio range of 0.4 – 1.5;

TNF- $\alpha$  to IL-2 at a ratio range of 3.2 – 10.9;

IFN- $\gamma$  to IL-2 at a ratio range of 1.5 – 10.9; and

GM-CSF to IL-2 at a ratio range of 2.2 – 4.8.

22. The method of claim 21, wherein said specific ratios of cytokines are as follows:

IL-1 $\beta$  to IL-2 at a ratio range of 0.6 to 0.8;

TNF- $\alpha$  to IL-2 at a ratio range of 7.7 to 11.3;

IFN- $\gamma$  to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

23. The method of claim 13 wherein the serum-free and mitogen-free cytokine mixture is Multikine®.

24. A serum-free and mitogen-free cytokine mixture, comprising specific ratios of cytokines selected from the group of IL-1 $\beta$ , TNF- $\alpha$ , IFN- $\gamma$  and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1 $\beta$  to IL-2 at a ratio range of 0.4 – 1.5;

TNF- $\alpha$  to IL-2 at a ratio range of 3.2 – 10.9;

IFN- $\gamma$  to IL-2 at a ratio range of 1.5 – 10.9; and

GM-CSF to IL-2 at a ratio range of 2.2 – 4.8.

25. The serum-free and mitogen-free cytokine mixture of claim 24, wherein said specific ratios of cytokines are as follows:

IL-1 $\beta$  to IL-2 at a ratio range of 0.6 to 0.8;

TNF- $\alpha$  to IL-2 at a ratio range of 7.7 to 11.3;

IFN- $\gamma$  to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

26. A pharmaceutical composition for use in treating cancer, comprising specific ratios of cytokines selected from the group of IL-1 $\beta$ , TNF- $\alpha$ , IFN- $\gamma$  and GM-CSF to Interleukin-2 (IL-2) as follows:

IL-1 $\beta$  to IL-2 at a ratio range of 0.4 – 1.5;

TNF- $\alpha$  to IL-2 at a ratio range of 3.2 – 10.9;

IFN- $\gamma$  to IL-2 at a ratio range of 1.5 – 10.9;

GM-CSF to IL-2 at a ratio range of 2.2 – 4.8, and optionally in combination with a pharmaceutically acceptable excipient, carrier or additive..

27. The pharmaceutical composition of claim 26, wherein said specific ratios of cytokines are as follows:

IL-1 $\beta$  to IL-2 at a ratio range of 0.6 to 0.8;

TNF- $\alpha$  to IL-2 at a ratio range of 7.7 to 11.3;

IFN- $\gamma$  to IL-2 at a ratio range of 4.9 to 7.1; and

GM-CSF to IL-2 at a ratio range of 3.5 to 4.5.

28. The pharmaceutical composition of claim 27, further comprising an IL-3 to IL-2 ratio in a range from 0.38 – 0.68, preferably at 0.53+/- 0.15
29. The pharmaceutical composition of claim 27, further comprising an IL-6 to IL-2 ratio in a range from 37.2 – 53.8, preferably at 46+/- 5.9.
30. The pharmaceutical composition of claim 27, further comprising an IL-8 to IL-2 ratio in a range from 261 – 561.5, preferably at 41+/- 10.6.
31. The pharmaceutical composition of claim 27, further comprising an IL-1 $\alpha$  to IL-2 ratio in a range from 0.56 – 0.94, preferably at 0.75+/- 0.19.
32. The pharmaceutical composition of claim 27, further comprising an IL-10 to IL-2 ratio in a range from 2.87 – 3.22, preferably at 3.0+/- 0.18.
33. The pharmaceutical composition of claim 27, further comprising an IL-16 to IL-2



ratio in a range from 1.24 – 2.84, preferably at 1.84+/-0.68.

34. The pharmaceutical composition of claim 27, further comprising a G-CSF to IL-2 ratio in a range from 2.16 – 3.78, preferably at 2.97+/- 0.81.
35. The pharmaceutical composition of claim 27, further comprising a TNF- $\beta$  to IL-2 ratio in a range from 1.18 – 2.43, preferably at 1.8+/- 0.63.
36. The pharmaceutical composition of claim 27, further comprising a MIP-1 $\alpha$  to IL-2 ratio in a range from 16.78 – 37.16, preferably at 22.7+/- 7.0.
37. The pharmaceutical composition of claim 27, further comprising a MIP-1 $\beta$  to IL-2 ratio in a range from 19.2 – 26.4, preferably at 22.8+/- 5.7.
38. The pharmaceutical composition of claim 27, further comprising a RANTES to IL-2 ratio in a range from 2.3 – 2.7, preferably at 2.5+/- 0.13.
39. The pharmaceutical composition of claim 27, further comprising a EGF to IL-2 ratio in a range from 0.27 – 0.28, preferably at 0.275+/- 0.008.
40. The pharmaceutical composition of claim 27, further comprising a PGE<sub>2</sub> to IL-2

ratio in a range from 3.68 – 5.42, preferably at 4.5+/- 0.87.

41. The pharmaceutical composition of claim 27, further comprising a TxB<sub>2</sub> to IL-2 ratio in a range from 23.5 – 25.1, preferably at 24.3+/- 0.83.